Cancer and Cancer treatments on cognition: A major translational impact of the preclinical research

Par

Hélène CASTEL

(Invitée par Virginie DESESTRET)

Normandie Rouen University
Inserm 1239 – Team Astrocyte and Vascular Niche
76821 Mont-Saint-Aignan cedex

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Salle Guillermond
Bât. L’Herbier
9, rue Raphaël DUBOIS
69100 Villeurbanne - Domaine Universitaire de La Doua
Abstract:

Co-head Cancer and Neurosciences axis Northwest canceropole, Cancer and cognition platform; ICCTF member (editing of preclinical research guidelines).

The emergence of a new field in oncology addressing cognitive deficits in cancer patients is justified by the existence of deficits in memory, concentration and attention, as well as executive functions before, during and after treatments, symptoms often referring to the “chemofog” or “cancerfog”. Our work mainly involves research and clinical groups of Normandie developing programs in patients and animal models, to improve our understanding of the impact of cancer and its treatments on cognitive functions. Two main examples of these translational studies we participated on can be exposed:

The first Cog-Age clinical study (Pr F. Joly, Baclesse Caen) showed that cognitive decline can be detected 6 months after chemotherapy in breast cancer elderly patients. In a mirror study, chemotherapy administration in young and elderly mice resulted in a change in behavioral flexibility and alteration of neuron precursor proliferation in the hippocampal dentate gyrus. We were thus able to conclude that age-related cognitive decline is accentuated by chemotherapy, providing basis for questioning the place of adjuvant chemotherapy in this elderly patient population. The second clinical study COG-ANGIO (Pr Joly) demonstrated that antiangiogenics exert a direct negative impact on cognitive functions and fatigue in kidney cancer patients.

In mice, the anti-angiogenic mTOR inhibitor everolimus did not alter cognitive functions but led to weight loss and modification of cell metabolism in brain regions involved in sleep/wake cycle or food intake, likely connected to fatigue. On the other hand, immunoneutralizing VEGF (Genentech-Roche, MTA) impaired spatial learning performance and neuronal activity of CA3 hippocampus neurons. These data suggest that a careful and systematic evaluation of targeted cancer therapies on cognitive functions in preclinical models may constitute a strategy of prevention by selection of treatments exhibiting minimum brain co-morbidities.

Together, this translational program is developed within the National Cancer and Cognition Platform (CNO/Ligue Nationale contre le cancer), with the aim to collaborate in a structured way with French oncology groups, research teams as well as pharmaceutical industry, by providing preclinical models and guidance on standard operating procedures for ancillary or future studies in identified population at risk.

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